

II. Specification

The specification has been amended so that the tradename "Tazarotène™" is accompanied by the complete generic chemical name in accordance with U.S. practice set forth in M.P.E.P. § 608.01(v). The trade name "Tazarotène™" appeared in the originally filed national phase application, filed under 35 U.S.C. § 371, and subsequently filed in the U.S.. The complete chemical name for "Tazarotene™" is 6-[(3,4-dihydro-4,4-dimethyl-2H-1-benzothiopyran-6-yl)ethylnyl]-3-pyridinecarboxylic acid ethyl ester, as shown by the attached Merck Index citation, see page 1554, compound 9249. Accordingly, this amendment contains no new matter.

III. Rejection of Claims 39 and 55 Under 35 U.S.C. § 112

The Examiner rejected claims 39 and 55 under 35 U.S.C. § 112, second paragraph, as allegedly indefinite, on the asserted grounds that certain of the listed compounds are not retinoids. Applicant respectfully traverses this rejection.

Attached hereto is a citation from the Merck Index identifying the full chemical name of Tazarotene™, which defines it as a "synthetic acetylenic retinoid." Also attached is an article from *Pharmacology of Retinoids in the Skin*, by M. Darmon, et al. (1989), in which 2-(5,6,7,8-tetrahydro-5,5,8,8-tetramethyl-2-naphthyl)-6-benzo[b]thiophenecarboxylic acid and 6-[3-(1-adamantyl)-4-methoxyphenyl]-2-naphthanoic acid are described as retinoids. See page 57, Fig. 1, formulas II and IV. Accordingly, Applicant submits that one of ordinary skill in the art reading the

specification as filed would have recognized that the recited compositions are each appropriately classified as retinoids.

Finally, in an effort to clarify the disclosure regarding "Tazarotene™", claims 39 and 55 have been replaced with new claims 65 and 66 in order to recite the complete chemical name for "Tazarotene™," in accordance with the specification. Again, no issue of new matter is raised by these amendments. Furthermore, these amendments are not made for purposes of overcoming any of the prior art. Accordingly, applicant respectfully requests that this rejection be withdrawn as it has been overcome.

**IV. Rejection of Claims 31-34, 43-45 and 59-61 Under
35 U.S.C. § 103(a) as Unpatentable Over Teale in View of Williamson**

The Examiner has rejected claims 31-34, 43-45 and 59-61 as unpatentable over Teale in view of Williamson for the reasons given at pages 2-3 of the Office Action. This rejection is respectfully traversed.

To establish a *prima facie* case of obviousness, the prior art relied upon, coupled with the knowledge generally available in the art at the time of the invention, must contain some suggestion or incentive that would have motivated the skilled artisan to modify a reference or to combine references. See *In re Fine*, 837 F.2d 1071, 1074, 5 U.S.P.Q.2d 1596, 1598 (Fed. Cir. 1988); *In re Skinner*, 2 U.S.P.Q.2d 1788, 1790 (Bd. Pat. App. & Int. 1986). The combination of the teachings of Teale and Williamson fails to provide the necessary motivation, and is improperly based on pure hindsight.

Teale teaches a pharmaceutical composition comprising an NO synthase inhibitor in combination with an anti-inflammatory agent. Teale, however, fails to teach or suggest a composition which comprises an NO synthase inhibitor in combination with a component that is capable of causing cutaneous irritation. The Examiner relies on Williamson in an attempt to satisfy this deficiency, i.e., for its teaching of conditions associated with cutaneous irritation. However, nothing in Teale or Williamson teaches that products used topically in the cosmetic or pharmaceutical field cause a cutaneous irritant effect. Even assuming, *arguendo*, that such irritant effects are known in the prior art (since they are clearly not learned from these references), nothing in either of the references suggests that a particular cutaneous irritant effect arising from these products is, or even could be, counteracted by the presence of an NO synthase inhibitor. This is the discovery of the present inventors. Thus, Applicant has shown that the Examiner has not made a *prima facie* case of obviousness and respectfully requests that this rejection be withdrawn.

V. Rejections of Claims 35 and 51 Under 35 U.S.C. § 103(a)
as Unpatentable Over Teale in View of Wilhelm and Williamson

The Examiner rejected claims 35 and 51 as unpatentable over Teale in view of Wilhelm and Williamson for the reasons given at page 3 of the Office Action. Applicant respectfully traverses this rejection.

The addition of Wilhelm to the teachings of Teale and Williamson does not supply the motivation identified above as being absent. Wilhelm merely discloses that

certain surfactants cause skin irritation. Wilhelm does not suggest, much less teach, that adding an NO synthase inhibitor to a composition comprising a surfactant reduces the cutaneous irritant effect of the surfactant.

Further, Applicant seeks clarification regarding the Examiner's statement in paragraph 2 of the Office Action, " . . . surfactants may lead to the production of nitric oxide by stimulating nitric oxidase (as taught by Williamson et al.) . . ." Applicant does not see this teaching in Williamson. Accordingly, the combination of Wilhelm with Teale and Williamson is not only not suggested by information in the references, but, fails to achieve the presently claimed invention. In view of the foregoing remarks, Applicant has demonstrated that the Examiner has failed to establish a *prima facie* case of obviousness. This rejection should therefore be withdrawn.

VI. Rejections of Claims 36-39, 47, 52-55, 63 and 64 Under
35 U.S.C. § 103(a) as Unpatentable Over Yu in View of Williamson

The Examiner has rejected claims 36-39, 47, 52-55, 63 and 64 as unpatentable over Yu in view of Williamson for the reasons given at pages 3-4 of the Office Action. Applicant respectfully traverses this rejection.

Assuming, for the sake of argument, that the Examiner has correctly characterized the references individually, the rejection continues to be deficient because it fails to identify any motivation found in the prior art, or known to one of ordinary skill in the art, that would have led to the combination of references. Yu identifies lowered pH as the cause of possible skin inflammation, and nowhere

mentions the use of NO synthase inhibitors to combat the problem. Nothing in the references of record suggests that NO synthase inhibitors are effective to combat the problem of skin inflammation caused by the low pH of the compounds identified in Yu. Williamson is directed instead to the "prevention/treatment of a broad spectrum of diseases which may be linked to the production of nitric oxide by leukocytes (neutrophils and macrophages) and other cells of non hemopoietic origin. . . ." (col. 3, lines 14-16). Williamson never mentions irritation caused by cosmetic products, and never suggests that NO synthase inhibitors are effective to address that problem. Therefore, the Examiner has failed to make a *prima facie* case of obviousness, and this rejection should be withdrawn.

VII. Rejections of Claims 45, 46, 61 and 62 Under
35 U.S.C. § 103(a) as Unpatentable Over Teale in View of Ahluwalia

The Examiner has also rejected claims 45, 46, 61 and 62 as unpatentable over Teale in view of Ahluwalia for the reasons found at page 5 of the Office Action. Applicant respectfully traverses this rejection.

Ahluwalia discloses certain nitric oxide synthase inhibitors claimed, but Ahluwalia discloses these compounds as being useful for the removal of hair. Nothing in the art of record, much less in the Examiner's rejection, suggests why it would have been obvious that these same compounds would have been useful as a component in a cosmetic or pharmaceutical composition in combination with a skin irritating component as claimed. Accordingly, this rejection, as each of the previous Rejections, fails to

support a *prima facie* case of obviousness. Applicant respectfully requests that this rejection be withdrawn.

The critical teaching missing from all of the references cited by the Examiner is the teaching that a cosmetic composition containing a skin irritating component can be advantageously improved, e.g., less irritating when applied to the skin, etc., by adding an NO synthase inhibitor. Without that teaching, or at least something that would have made such a combination obvious to one of ordinary skill in the art, the cited references do not support a *prima facie* case of obviousness.

In view of the foregoing amendments and remarks, Applicant respectfully requests the reconsideration and reexamination of the pending claims and the timely allowance of the pending claims.

To the extent any extension of time under 37 C.F.R. § 1.136 is required to obtain entry of this Amendment, such extension is hereby requested. If there are any fees due under 37 C.F.R. § 1.16 or 1.17 which are not enclosed, including any fees required for an extension of time under 37 C.F.R. § 1.136, please charge those fees to our Deposit Account No. 06-0916.

Respectfully submitted,

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